

N-Methyl-N-Nitroso-1-Alkylamines and

N-Methyl-N-Nitroso-1-Octanamine (MNOA)

N-methyl-N-nitrosooctylamine; nitrosomethyl-n-octylamine

N-Methyl-N-Nitroso-1-Decanamine (MNDeA)

N-methyl-N-nitrosodecylamine; nitrosomethyl-n-decylamine

N-Methyl-N-Nitroso-1-Dodecanamine (MNDodeA)

N-methyl-N-nitrosododecylamine; nitrosomethyl-n-dodecylamine

N-Methyl-N-Nitroso-1-Tetradecanamine (MNTA)

N-methyl-N-nitrosotetradecylamine; nitrosomethyl-n-tetradecylamine

N-Methyl-N-nitroso-1-alkylamines are contaminants found in some hair care products, household dishwashing liquids and surface cleaners. These compounds are not intentionally added to these products, but may form as a result of the reaction of nitrite with amine compounds.

- N-Methyl-N-nitroso-1-octanamine has been detected in hair care products such as shampoos and conditioners that are formulated with lauramine oxide. It is formed as a result of reactions of nitrite with diethanolamine and triethanolamine.
- N-Methyl-N-nitroso-1-decanamine has not been reported in consumer products. It is one of several nitroso compounds theorized to possibly “have some human exposure.” (Personal communication, Dr. William Lijinsky, 1995).
- N-Methyl-N-nitroso-1-dodecanamine is found in household dishwashing liquids and surface cleaners, and in hair care products such as shampoo.
- N-Methyl-N-nitroso-1-tetradecanamine is found in hair care products.

Exposure to N-methyl-N-nitroso-1-alkylamines may occur to consumers who use hair care products, dishwashing liquids, or surface cleaners containing these contaminants.

N-Methyl-N-nitroso-1-alkylamines as a chemical group and four individual compounds in the group (*i.e.*, MNOA, MNDeA, MNDodeA, and MNTA) passed the animal data screen, underwent a preliminary toxicological evaluation, and are being brought to the Carcinogen Identification Committee (CIC) for consultation. This is a compilation of the relevant studies identified during the preliminary toxicological evaluation.

Epidemiological data

No cancer epidemiology studies on N-methyl-N-nitroso-1-alkylamines were identified.

Animal carcinogenicity data

Table 1. Treatment-related findings in rodent studies with N-Methyl-N-nitroso-1-alkylamines

| Chemical | Animal tumor data | References |
|---|--|----------------------------|
| <p>N-Methyl-N-nitroso-1-ethanamine (N-Nitrosomethylethylamine) Proposition 65 carcinogen</p> | <p>23-30-week gavage (1X/week) study in male Syrian hamsters (observed for life)</p> <ul style="list-style-type: none"> • <i>Increases in liver, nasal and tracheal tumors</i> | Lijinsky and Kovach (1988) |
| <p>N-Methyl-N-nitroso-1-propanamine</p> | <p>23-30-week gavage (1X/week) studies in male and female Syrian hamsters (observed for life)</p> <ul style="list-style-type: none"> • <i>Increases in liver, lung and nasal tumors in males</i> • <i>Increases in liver and nasal tumors in females</i> | Lijinsky and Kovach (1988) |
| <p>N-Methyl-N-nitroso-1-butanamine</p> | <p>23-30-week gavage (1X/week) studies in male and female Syrian hamsters (observed for life)</p> <ul style="list-style-type: none"> • <i>Increases in liver, lung, forestomach and nasal tumors in males and females</i> | Lijinsky and Kovach (1988) |
| <p>N-Methyl-N-nitroso-1-pentanamine (nitrosomethylamylamine)</p> | <p>23-30-week gavage studies in male and female Syrian hamsters (observed for life)</p> <ul style="list-style-type: none"> • <i>Increases in liver, lung, forestomach and nasal tumors in males and females</i> | Lijinsky and Kovach (1988) |

| | | |
|--|---|--|
| <p>N-Methyl-N-nitroso-1-hexanamine</p> | <p>50-week gavage studies in male and female Syrian hamsters (observed for life)</p> <ul style="list-style-type: none"> • <i>Increases in liver, lung, forestomach, nasal and bladder tumors in males</i> • <i>Increases in liver, lung, forestomach and bladder tumors in females</i> | <p>Lijinsky and Kovach (1988)</p> |
| <p>N-Methyl-N-nitroso-1-heptanamine</p> | <p>40-week gavage studies in male and female Syrian hamsters (observed for life)</p> <ul style="list-style-type: none"> • <i>Increases in liver, lung, forestomach and nasal tumors in males and females</i> | <p>Lijinsky and Kovach (1988)</p> |
| <p>N-Methyl-N-nitroso-1-octanamine</p> | <p>30-week gavage (2X/week) study in male Fischer rats (observed for life)</p> <ul style="list-style-type: none"> • <i>Increases in liver, bladder, lung and nasal cavity tumors</i> <p>40-week gavage (1X/week) studies in male and female Syrian hamsters (observed for life)</p> <ul style="list-style-type: none"> • <i>Increases in liver, lung, forestomach, nasal, and bladder tumors in males and females</i> | <p>Lijinsky <i>et al.</i> (1981)</p> <p>Lijinsky and Kovach (1988)</p> |
| <p>N-Methyl-N-nitroso-1-nonanamine</p> | <p>30-week gavage (2X/week) study in male Fischer rats (observed for life)</p> <ul style="list-style-type: none"> • <i>Increases in liver, lung and nasal cavity tumors</i> | <p>Lijinsky <i>et al.</i> (1981)</p> |
| <p>N-Methyl-N-nitroso-1-decanamine</p> | <p>30-week gavage (2X/week) study in male Fischer rats (observed for life)</p> <ul style="list-style-type: none"> • <i>Increases in bladder and lung tumors</i> | <p>Lijinsky <i>et al.</i> (1981)</p> |

| | | |
|---|--|-------------------------------|
| N-Methyl-N-nitroso-1-dodecanamine | 50-week studies gavage (2X/week) in male and female Sprague-Dawley rats | Lijinsky and Taylor (1975) |
| | <ul style="list-style-type: none"> • <i>100% incidence of transitional cell carcinoma of urinary bladder, with some metastasis to the lungs, in males and females</i> | |
| | 30-week study gavage (2X/week) in male Fischer rats (observed for life) | Lijinsky <i>et al.</i> (1981) |
| | <ul style="list-style-type: none"> • <i>Increases in bladder, lung, forestomach, and pancreatic islet cell tumors</i> | |
| | Gavage studies (1X/week for life) in male and female Syrian hamsters | Althoff and Lijinsky (1977) |
| | <ul style="list-style-type: none"> • <i>Increase in urinary tract tumors in males</i> • <i>Increase in urinary tract and respiratory tract tumors in females</i> | |
| | Subcutaneous injection studies (1X/week for life) in male and female European hamsters | Kektar <i>et al.</i> (1981) |
| | <ul style="list-style-type: none"> • <i>Increases in lung and urinary bladder tumors in males and females</i> | |
| | 40-week gavage (2X/week) study in male guinea pigs (observed for life) | Cardy and Lijinsky (1980) |
| | <ul style="list-style-type: none"> • <i>Increases in angiosarcoma of liver and bile duct carcinoma</i> | |
| N-Methyl-N-nitroso-1-tetradecanamine | 30-week gavage (2X/week) study in male Fischer rats (observed for life) | Lijinsky <i>et al.</i> (1981) |
| | <ul style="list-style-type: none"> • <i>Increases in bladder tumors (100% incidence)</i> | |

Other relevant data

- Genotoxicity: See Table 2.

Table 2. Mutagenicity in *Salmonella typhimurium* (Andrews and Lijinsky, 1980)

| Chemical | Results |
|---|-----------------|
| N-Methyl-N-nitroso-ethylamine (N-Nitrosomethylethylamine) Proposition 65 carcinogen | <i>negative</i> |
| N-Methyl-N-nitroso-propylamine | <i>positive</i> |
| N-Methyl-N-nitroso-butylamine | <i>positive</i> |
| N-Methyl-N-nitroso-neopentylamine | <i>negative</i> |
| N-Methyl-N-nitroso-hexylamine | <i>positive</i> |
| N-Methyl-N-nitroso-heptylamine | <i>positive</i> |
| N-Methyl-N-nitroso-octanamine | <i>positive</i> |
| N-Methyl-N-nitroso-nonylamine | <i>positive</i> |
| N-Methyl-N-nitroso-decanamine | <i>positive</i> |
| N-Methyl-N-nitroso-undecylamine | <i>positive</i> |
| N-Methyl-N-nitroso-dodecanamine | <i>positive</i> |

- Structure-activity considerations
 - Similarity to numerous mutagenic and carcinogenic N-nitroso compounds and nitrosamines: IARC (1978); Andrews *et al.* (1978)
 - Similarity to 23 Proposition 65 carcinogen nitroso compounds, including 16 nitrosamines:
 - N-Nitrosomethylethylamine
 - N-Carboxymethyl-N-nitrosourea
 - 1-(2-Chloroethyl)-3-cyclohexyl-1-nitrosourea
 - N-Methyl-N'-nitro-N-nitrosoguanidine
 - N-Nitrosodi-*n*-butylamine
 - N-Nitrosodiethanolamine
 - N-Nitrosodiethylamine
 - N-Nitrosodimethylamine
 - *p*-Nitrosodiphenylamine
 - N-Nitrosodiphenylamine

- N-Nitrosodi-n-propylamine
- N-Nitroso-N-ethylurea
- 3-(N-Nitrosomethylamino)-1-(3-pyridyl)1-butanone
- N-Nitroso-N-methylurea
- N-Nitroso-N-methylurethane
- N-Nitroso-N-methylvinylamine

References¹

Althoff J, Lijinsky W (1977). Urinary bladder neoplasms in Syrian hamsters after administration of N-nitroso-N-methyl-N-dodecylamine. *Z Krebsforsch* **90**:227-231.

Andrews AW, Thibault LH, Lijinsky W (1978). The relationship between mutagenicity and carcinogenicity of some nitrosamines. *Mutat. Res.* **51**:319-326.

Andrews AW, Lijinsky W (1980). The mutagenicity of 45 nitrosamines in *Salmonella typhimurium*. *Teratog Carcinog Mutagen* **1**(3):295-303.

Cardy RH, Lijinsky W (1980). Comparison of the carcinogenic effects of five nitrosamines in guinea pigs. *Cancer Res* **40**:1879-1884.

International Agency for Research on Cancer (IARC, 1978). IARC Monograph on the Evaluation of Carcinogenic Risk to Humans: Some N-Nitroso Compounds. Volume 17. IARC, Lyon, France.

Kektar MB, Althoff J, Lijinsky W (1981). The carcinogenic effect of nitrosomethyldodecylamine in European hamsters. *Cancer Lett* **13**:165-168.

Lijinsky W, Taylor HW (1975). Induction of urinary bladder tumors in rats by administration of nitrosomethyldodecylamine. *Cancer Res* **35**:958-961.

Lijinsky W, Saavedra JE, Reuber MD (1981). Induction of carcinogenesis in Fischer rats by Methylalkylnitrosamines. *Cancer Res* **41**:1288-1292.

Lijinsky W, Kovach RM (1988). Comparative carcinogenesis by nitrosomethylalkylamines in Syrian hamsters. *Cancer Res* **48**:6648-6652.

¹ Excerpts or the complete publication have been provided to members of the Carcinogen Identification Committee, in the order in which they are discussed in this document.